20

25

5

10

ABSTRACT OF THE DISCLOSURE

DOPAMINE AGONIST FORMULATIONS FOR ENHANCED CENTRAL NERVOUS SYSTEM DELIVERY

Pharmaceutical formulations are described comprising at least one dopamine receptor agonist and one or more mucosal delivery-enhancing agents for enhanced mucosal delivery of the dopamine receptor agonist. In one aspect, the mucosal delivery formulations and methods provide enhanced delivery of the dopamine receptor agonist to the central nervous sytstem (CNS), for example by yielding dopamine receptor agonist concentrations in the cerebral spinal fluid of 5% or greater of the peak dopamine agonist concentrations in the blood plasma following administration to a mammalian subject. Exemplary formulations and methods within the invention utilize apomorphine as the dopamine receptor agonist. Other exemplary methods and formulations focus in intranasal administration of a dopamine receptor agonist. The formulations and methods of the invention are useful for treating a variety of diseases and conditions in mammalian subjects, including Parkinson's disease, male erectile dysfunction, female sexual dysfunction, among others. In alternate aspects, the mucosal delivery formulations and methods of the invention include one, or any combination of, mucosal delivery-enhancing agents selected from (a) aggregation inhibitory agents; (b) charge modifying agents; (c) pH control agents; (d) degradative enzyme inhibitors; (e) mucolytic or mucus clearing agents; (f) ciliostatic agents; (g) membrane penetrationenhancing agents; (h) modulatory agents of epithelial junction physiology; (i) vasodilator agents; (j) selective transport-enhancing agents; and (k) stabilizing delivery vehicles, carriers, supports or complex-forming agents. These methods and formulations of the invention provide for significantly enhanced absorption of dopamine receptor agonists into or across a nasal mucosal barrier to a target site of action, for example the CNS.

30 SE 5008850 v1